REMARKS

In this Amendment, claims 2-14 are amended, claims 21-29 are new, and claim 1 is canceled. Additionally, claims 15-20 which were withdrawn as being directed to a non-elected invention, are also canceled. Applicants reserve the right to file one or more divisional application directed to the inventions of claims 15-20.

After entry of this Amendment, claims 1-14, and 21-28 are pending in the application.

New claims 21 and 22 are added in place of claim 1. Claims 21 and 22 recite that the first and second ligands may be protein phosphatase enzymes as described in the specification at page 7, lines 33-36, and the paragraph bridging pages 7 and 8. Claims 21 and 22 are otherwise supported by the original claims and pages 4 and 5 of the specification.

Further with respect to claims 21 and 22, these claims recite qualitative assays, as supported by original claim 5, which has been amended to recite a quantitative assay. See the paragraph bridging pages 4 and 5 of the specification.

Claims 23 and 24 are directed to embodiments where the immobilized ligand is indirectly or directly immobilized to the solid support, respectively. Support is found, for example, in the specification in Examples 1-3.

Claims 25 and 26 are directed to embodiments where the presence of the second ligand in a fraction is determined directly or indirectly, respectively. Support can be found for claims 25 and 26 at page 4, lines 34-37 of the specification.

Claims 27 and 28 are directed to embodiments where the presence of the second ligand in a fraction is directly or inversely related to the presence of the toxin in the sample. Support can be found for claims 27 and 28 at page 5, lines 15-24 of the specification.

Claim 29 recites an embodiment where both the first ligand and the second ligand are protein phosphatase enzymes. Claim 29 is supported by pages 7 and 8 of the specification.

For example, the specification states that "preferably the toxin binding ligand of the invention is a protein phosphatase enzyme...Likewise, the second ligand used in the method of the invention may be any ligand which binds to the toxin either competitively or non-competitively with the first ligand...Preferably the first ligand is a toxin binding ligand, more preferably a protein phosphatase enzyme."

Claims 2-14 have been amended to change the dependency as necessitated by the new independent claims, and to use terminology consistent with the new independent claims.

The remainder of the claim amendments are merely editorial in nature and are intended to impart clarity to the claims. As such, these amendments are not narrowing.

No new matter has been introduced.

Entry of the Amendment is respectfully requested.

Election of Group I, Claims 1-14

The Examiner requests that Applicants affirm the election of Group I, claims 1-14.

Accordingly, Group I, claims 1-14 are elected for prosecution. Non-elected claims 15-20 are canceled without prejudice to the filing of a divisional application thereon.

Response to Claim Rejections Under 35 USC § 112, Second Paragraph

Claims 1-14 are rejected under 35 USC § 112, second paragraph, as being indefinite.

Specifically, the Examiner appears to find the relationships between the various components and steps of the assay to be unclear. Particularly, the Examiner states that claim 1 does not require that either the immobilized or non-immobilized ligand bind to a toxin, and the Examiner states that in claim 1, if step (i) and (ii) are performed separately, it is not clear that the non-immobilized ligand and the phosphatase-targeting toxin would contact each other as may be required by the claims.

Claim 1 has been canceled and replaced with independent claims 21 and 22, which are directed to competition and sandwich assay formats, respectively. Both assay formats had been encompassed by claim 1. It is believed that claims 21 and 22 more clearly recite the relationships between the assay components, as well as between the steps of the method. It should be noted that the steps of the assay can be performed in various orders, and it will be evident to one of ordinary skill in the art the operable ordering of the steps.

In view of new claims 21 and 22, Applicants respectfully request withdrawal of this rejection.

Response to Claim Rejections Under 35 USC §102

(1) The Examiner rejects claims 1, 4, 7 and 13 under 35 USC §102(b) as being anticipated by Usagawa et al (1989).

Specifically, the Examiner states that Usagawa teaches a competitive immunoassay using okadaic acid coupled to a support. The Examiner states that the method of Usagawa tests for the

ability of an antibody directed against okadaic acid to bind to the immobilized okadaic acid in the presence of non-immobilized okadaic acid.

(2) The Examiner rejects claims 1-5, 10 and 14 under 35 USC §102(b) as being anticipated by Sikorska et al (US 5,264,556).

Specifically, the Examiner states that Sikorska teaches an assay involving immobilized antibody directed against okadaic acid (6/50 IgG), an unbound anti-idiotypic antibody against 6/50 IgG (1/59 IgG), and unbound okadaic acid, where free okadaic acid inhibits the binding of anti-idiotypic 1/59 IgG to solid phase bound 6/50 IgG.

New independent claims 21 and 22 recite that at least one of the first ligand and the second ligand is a protein phosphatase capable of binding the phosphatase-targeting toxin. On the other hand, neither Usagawa nor Sikorska discloses a method employing a protein phosphatase capable of binding the phosphatase targeting toxin.

It is submitted that the alkaline phosphatase enzyme disclosed by Usagawa, as an enzymatic label attached to a secondary antibody, is not a protein phosphatase capable of binding the phosphatase targeting toxin as is recited in the instant claims.

In view of the above, withdrawal of this rejection is respectfully requested.

Response to Claim Rejections Under 35 USC §103

The Examiner rejects claims 1-3, 5, 6, 8 and 9 under 35 USC §103(a) as being obvious over Holmes (US 5,180,665) in view of Maggio (1980).

Specifically, the Examiner states that Holmes teaches a method for quantitatively assaying the presence of diarrhetic shellfish poisoning (DSP) toxins, such as okadaic acid. The Examiner states that the method of Holmes comprises the steps of preparing a marine extract, fractionating the prepared marine extract, selecting the extract fraction containing toxin, contacting a labeled substrate for protein phosphatase and at least one protein phosphatase to the extract in an assay.

The Examiner admits that Holmes does not teach immobilization of a ligand to a solid support.

However, the Examiner states that Maggio teaches that, in order to quantify the amount of analyte present in an enzyme-immunoassay, the extent of reaction of the enzyme-labeled ligand with antibody must be determined, and such requires a physical separation of the free and antibody-bound fractions. The Examiner further contends that Maggio teaches that, in order to maximize precision and sensitivity, one would like to ensure complete separation of the free and bound fractions, such as by solid phase separation.

The Examiner concludes that it would have been obvious to modify the method of Holmes by immobilizing one of the ligands to a solid support, in order to ensure complete separation of the free and bound labels and thereby maximize the precision and sensitivity of the method as taught by Maggio.

This rejection is respectfully traversed as there is no motivation to combine these references.

As provide by Section 2143.01 (page 2100-132), the proposed modification cannot change the principle of operation of a reference. Citing the decision of *In re Ratti,* 270 F.2d 810; 123 USPQ 349 (CCPA 1959), the MPEP states: the suggested combination cannot "require a substantial reconstruction and redesign of the elements shown in the primary reference as well as a change in the basic principle under which the primary reference construction was designed to operate."

In the presently cited references, the assay of Holmes is an enzymatic assay while the assay of Maggio is a binding assay. More specifically, Holmes teaches measuring okadaic acid in a sample via its inhibitory effect on phosphatase enzymatic activity. Maggio, on the other hand, teaches immunoassays which detect the presence of components via antibody binding (which is not an enzymatic activity). The teachings of Maggio and Holmes operate on unrelated principles, and thus cannot be combined without a complete reconstruction of the Holmes assay, or without changing the fundamental principle upon which the Holmes assay is based (measuring phosphatase activity).

Said another way, based upon the teachings of Maggio and Holmes, there is no motivation to immobilize any component of an enzymatic assay. While physical separation of bound and unbound components may be appropriate for a binding assay, which operates through a physical capture of a component of interest, there is no suggestion provided by Maggio or Holmes that separating bound and unbound fractions would be beneficial in an enzymatic assay. An enzymatic assay does not operate through physical capture of a component, but operates through a determination of enzyme activity.

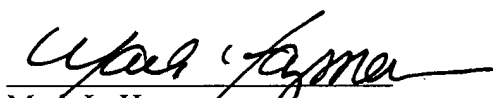
As there is no motivation to combine the cited references, none of the present claims are *prima facie* obvious. Withdrawal of this rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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